

## VERIFICATION OF TRANSLATION

I, **Hiroyuki Takano** of **721, Marunouchi-Nakadori bldg., 2-3, Marunouchi 2-chome, Chiyoda-ku, Tokyo, 100-0005 JAPAN**, am the translator of **Japanese Patent Application No. 2003-200674** and I state that the following is a true translation to the best of my knowledge and belief.

(Signature of Translator)

Hiroyuki Takano

Hiroyuki Takano

(Dated)

7 24, 2008

Translation of Japanese Patent Application No. 2003-200674

[Title of Document]      Application for Patent

[Docket No.] PA211-1115

[Address] Commissioner of the Japan Patent Office

[International Patent Classification] C07D233/14

5 B01J 31/02

C07B 53/00

[Inventor]

[Address] 20-39, Ichiriyama 3-chome, Ohtsu-shi, Shiga

[Name] MARUOKA Keiji

10 [Applicant]

[ID No.] 000003300

[Name] TOSOH CORPORATION

[Representative] TSUCHIYA Takashi

[Tel No.] (03) 5427-5134

15 [Filing Fee]

[Pre-payment Book No.] 003610

[Amount]        21,000 YEN

[List of Documents Filed]

[Title of Document]	Claims	1
---------------------	--------	---

20	[Title of Document]	Description	1
----	---------------------	-------------	---

[Necessity of Proof]      Necessary

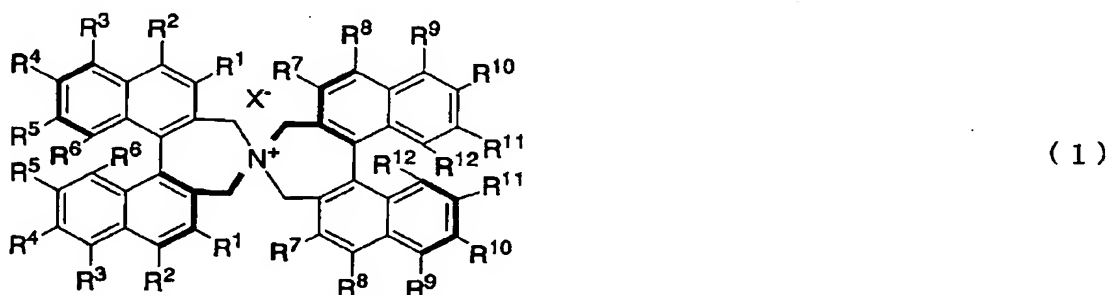
[TITLE OF DOCUMENT] DESCRIPTION

[TITLE OF THE INVENTION] FLUORINE-CONTAINING OPTICALLY ACTIVE  
QUATERNARY AMMONIUM SALT, PRODUCTION METHOD THEREOF, AND  
METHOD FOR PRODUCING OPTICALLY ACTIVE  $\alpha$ -AMINO ACID DERIVATIVE  
5 USING THE QUATERNARY AMMONIUM SALT

[CLAIMS]

[Claim 1] An optically active quaternary ammonium salt  
represented by the following general formula (1):

[Chemical Formula 1]



10 [wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> are  
each independently a hydrogen atom, a halogen atom, a methyl  
group that may or may not be substituted with fluorine, an  
ethyl group that may or may not be substituted with fluorine,  
15 a straight, branched or cyclic alkyl group that has 3 to 18  
carbon atoms and may or may not be substituted with fluorine,  
a straight, branched or cyclic heteroalkyl group that has 3 to  
18 carbon atoms and may or may not be substituted with  
fluorine, a straight, branched or cyclic alkenyl group that  
20 has 3 to 18 carbon atoms and may or may not be substituted  
with fluorine, a straight, branched or cyclic alkynyl group

that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, an alkoxy group that has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and may or may not be substituted with fluorine, an aralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine;

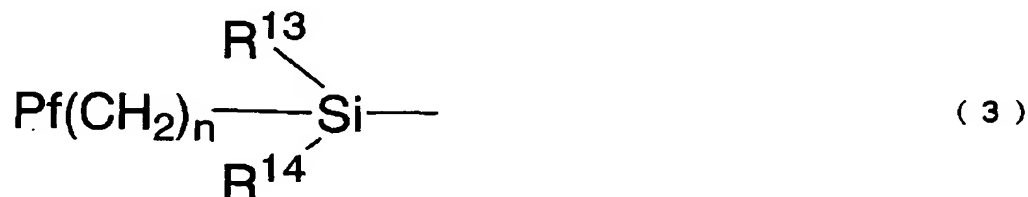
with the proviso that at least one of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ , and  $R^{12}$  is a substituent represented by the following general formula (2):

[Chemical Formula 2]



(wherein Pf is a straight, branched or cyclic alkyl group that has 2 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, or a heteroaralkyl

group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, and n is an integer from 0 to 4.), and/or by the following general formula (3):



5 (wherein Pf and n are as defined in the above general formula (2),  $\text{R}^{13}$  and  $\text{R}^{14}$  are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, 10 branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, a heteroaralkyl group having 5 to 25 carbon atoms, or the general formula above (2));

15  $\text{X}^-$  is a fluoride ion, a chloride ion, a bromide ion, an iodide ion, a p-toluenesulfonic acid ion, a hydroxide ion, a thiocyanate ion, a hydrogen sulfate ion, a perchloric acid ion, or a hexafluorophosphoric acid ion; and the two binaphthyl moieties each have a chiral axis so that the absolute 20 configurations of the two binaphthyl moieties are (R, R) or (S, S)].

[Claim 2] The chemical compound according to claim 1, wherein  $\text{R}^1$  and  $\text{R}^7$ ,  $\text{R}^3$  and  $\text{R}^9$ ,  $\text{R}^4$  and  $\text{R}^{10}$ ,  $\text{R}^5$  and  $\text{R}^{11}$ , and  $\text{R}^6$  and

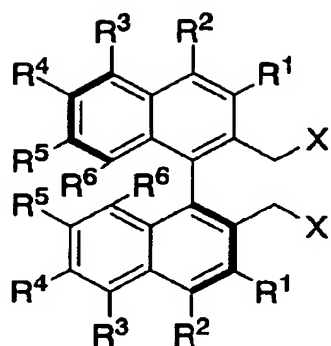
$R^{12}$  in the above general formula (1) are in each case identical to one another;  $R^2$  and  $R^8$  are identical to one another and are each represented by the above general formula (3); and  $X^-$  is a fluorine ion, a chloride ion, a bromide ion, an iodide ion, a p-toluenesulfonic acid ion, a thiocyanate ion, a hydrogen sulfate ion, or a hydroxide ion.

[Claim 3] The chemical compound according to claim 2, wherein  $R^1$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^9$ ,  $R^{11}$ , and  $R^{12}$  in the above general formula (1) are each independently a hydrogen atom;  $R^2$ ,  $R^4$ ,  $R^8$ , and  $R^{10}$  are identical to one another and are each represented by the above general formula (3); and  $X^-$  is a chloride ion, a bromide ion, an iodide ion, or a p-toluenesulfonic acid ion.

[Claim 4] The chemical compound according to claim 3, wherein in the general formula above (3),  $R^{13}$  and  $R^{14}$  are each a methyl group,  $n$  is 2,  $Pf$  is an  $n$ -octyl group having all the hydrogen atoms substituted with fluorine atoms, and  $X^-$  is a bromide ion.

[Claim 5] An optically active binaphthyl compound represented by the following general formula (4):

[Chemical Formula 4]



(4)

[wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are each independently a hydrogen atom, a halogen atom, a methyl group that may or may not be substituted with fluorine, an ethyl group that may or may not be substituted with fluorine, a straight, branched or cyclic alkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic heteroalkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, an alkoxy group that has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and may or may not be substituted with fluorine, an aralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine; with the proviso that at least one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>,

R<sup>5</sup> and R<sup>6</sup> is a substituent represented by the above general formula (2) or above general formula (3). X is a chlorine atom, a bromine atom, an iodine atom, or a p-toluenesulfonyloxy group; and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

[Claim 6] The chemical compound according to claim 5, wherein in the above general formula (4), R<sup>1</sup>, R<sup>3</sup>, R<sup>5</sup>, and R<sup>6</sup> are each independently a hydrogen atom, R<sup>2</sup> and R<sup>4</sup> are identical to one another and are each represented by the above general formula (3).

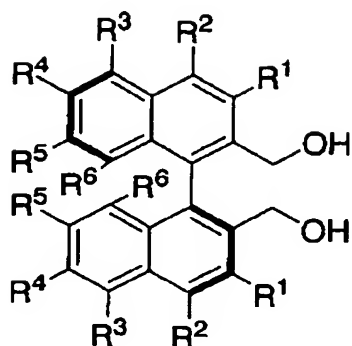
[Claim 7] The chemical compound according to claim 6, wherein the above general formula (3), R<sup>13</sup> and R<sup>14</sup> are each a methyl group, Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms, n is 2 and X is a bromine atom.

[Claim 8] A method for producing the chemical compound according to any of claims 1 to 4 represented by the above general formula (1) in which X<sup>-</sup> is a chloride ion, a bromide ion, a iodide ion, or a p-toluenesulfonic acid ion, characterized in that the optically active binaphthyl compound according to any of claims 5 to 7 represented by the above general formula (4) is reacted with ammonia.

[Claim 9] An optically active binaphthyl dihydroxyl compound represented by the following general formula (5):

[Chemical Formula 5]





( 5 )

[wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , and  $R^6$  are each as defined in the claim 5 represented by the general formula (3), and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

[Claim 10] The chemical compound according to claim 9, wherein  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  in the above general formula (5) are each independently a hydrogen atom; and  $R^2$  and  $R^4$  are identical to one another and are each represented by the above general formula (3).

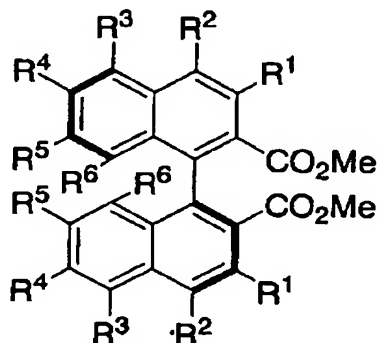
[Claim 11] The chemical compound according to claim 10, wherein in the above general formula (3)  $R^{13}$  and  $R^{14}$  are each a methyl group, and Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms, and n is 2.

[Claim 12] A method for producing the chemical compound of the above general formula (3) according to any of claims 5 to 7, characterized in that the chemical compound of the above general formula (5) according to any of claims 9 to 11 is reacted with a halogen source or p-toluenesulfonyl chloride.

[Claim 13] An optically active binaphthyl diester

compound represented by the following general formula (6):

[Chemical Formula 6]



[wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are each as defined in the  
 5 claim 5 represented by the general formula above (4), and the  
 binaphthyl moiety has a chiral axis so that the absolute  
 configuration of the binaphthyl moiety is (R) or (S)].

[Claim 14] The chemical compound according to claim 13,  
 wherein R<sup>1</sup>, R<sup>3</sup>, R<sup>5</sup>, and R<sup>6</sup> in the above general formula (6) are  
 10 each independently a hydrogen atom; and R<sup>2</sup> and R<sup>4</sup> are identical  
 to one another and are each represented by the above general  
 formula (3).

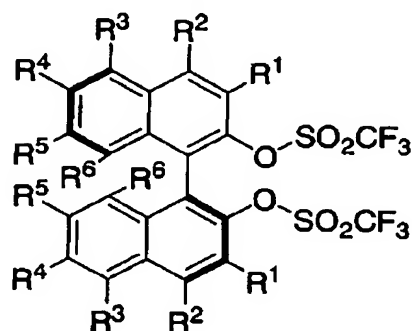
[Claim 15] The chemical compound according to claim 14,  
 wherein in the above general formula above (3), R<sup>13</sup> and R<sup>14</sup> are  
 15 each a methyl group, Pf is an n-octyl group having all the  
 hydrogen atoms substituted with fluorine atoms and n is 2,.

[Claim 16] A method for producing the compound according  
 to any of claims 9 to 11 represented by the above general  
 formula (5), characterized in that the chemical compound  
 20 according to any of claims 13 to 15 represented by the above

general formula (6) is reacted with hydrogen anion.

[Claim 17] An optically active binaphthyl compound represented by the following general formula (7):

[Chemical Formula 7]



( 7 )

[wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , and  $R^6$  are each as defined in the claim 5 represented by the general formula above (4), and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

[Claim 18] The chemical compound according to claim 17, wherein in the above general formula (7),  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each independently a hydrogen atom, and  $R^2$  and  $R^4$  are identical to one another and are each represented by the above general formula (3).

[Claim 19] The chemical compound according to claim 18, wherein in the above general formula (3),  $R^{13}$  and  $R^{14}$  are each a methyl group, Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms and n is 2,.

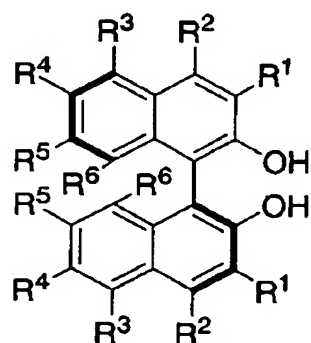
[Claim 20] A method for producing the chemical compound of the above general formula (6) according to any of claims 13 to 15, characterized in that the chemical compound of the

above general formula (7) according to any of claims 17 to 19 is reacted with carbon monoxide and methanol in the presence of a palladium catalyst and an organic base.

[Claim 21] An optically active binaphthol compound

5 represented by the following general formula (8):

[Chemical Formula 8]



(8)

[wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are each as defined in the claim 5 represented by the general formula above (4), and the  
10 binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

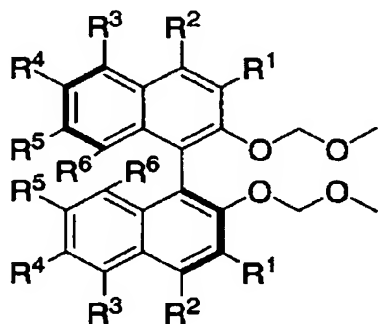
[Claim 22] The chemical compound according to claim 21, wherein R<sup>1</sup>, R<sup>3</sup>, R<sup>5</sup>, and R<sup>6</sup> in the above general formula (8) are each independently a hydrogen atom; and R<sup>2</sup> and R<sup>4</sup> are identical  
15 to one another and are each represented by the above general formula (3).

[Claim 23] The chemical compound according to claim 22, wherein in the above general formula (3), R13 and R14 are each a methyl group, Pf is an n-octyl group having all the hydrogen  
20 atoms substituted with fluorine atoms and n is 2.

[Claim 24] A method for producing the chemical compound according to any of claim 17 to 19 represented by the general above formula (7), characterized in that the chemical compound according to any of claims 21 to 23 represented by the above  
5 general formula (8) is reacted with a triflating agent.

[Claim 25] An optically active binaphthyl bis-methoxymethyl ether compound represented by the following general formula (9):

[Chemical Formula 9]



10 [wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are each as defined in the claim 5 represented by the general formula above (4), and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

15 [Claim 26] The chemical compound according to claim 25, wherein R<sup>1</sup>, R<sup>3</sup>, R<sup>5</sup>, and R<sup>6</sup> in the above general formula (9) are each independently a hydrogen atom; and R<sup>2</sup> and R<sup>4</sup> are identical to one another and are each represented by the above general formula (3).

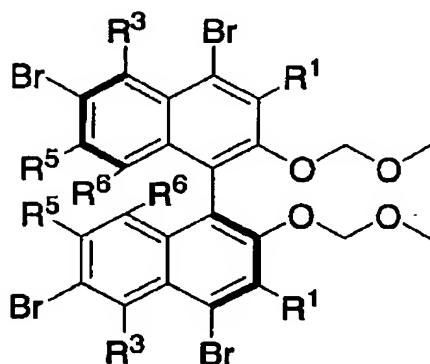
20 [Claim 27] The chemical compound according to claim 26, wherein in the above general formula (3), R<sup>13</sup> and R<sup>14</sup> are each a

methyl group, Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms and n is 2,.

[Claim 28] A method for producing the chemical compound according to any of claims 21 to 23 represented by the above  
5 general formula (8), characterized in that the chemical compound according to any of claims 25 to 27 represented by the above general formula above (9) is reacted with an acid.

[Claim 29] An optically active binaphthyl bis-methoxymethyl ether compound represented by the following  
10 general formula (10):

[Chemical Formula 10]



( 10 )

[wherein R<sup>1</sup>, R<sup>3</sup>, R<sup>5</sup>, and R<sup>6</sup> are each as defined in claim 5 represented by the above general formula (4), and the  
15 binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].  
And subsequently reacting with the reaction product a compound represented by the following general formula (11):

[Chemical formula 11]



[wherein Pf is a straight, branched or cyclic alkyl group that has 2 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a heteroaralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, n is an integer from 0 to 4, and R<sup>13</sup> and R<sup>14</sup> are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, a heteroaralkyl group having 5 to 25 carbon atoms, or a substituent represented by the general formula

(2).], a method for producing the chemical compound according to any of claims 25 to 27 represented by the above general formula above (9).

[Claim 30] In the presence of the chemical compound  
5 according to claim 1 to 4 represented by the above general formula above (1) and an inorganic base, the following general formula (12):

[Chemical Formula 12]



10 [wherein  $\text{R}^{15}$  and  $\text{R}^{16}$  are each independently a hydrogen atom or an aryl group that has 5 to 10 carbon atoms and may or may not be substituted with halogen, with the proviso that  $\text{R}^{15}$  and  $\text{R}^{16}$  are not a hydrogen atom at the same time;  $\text{R}^{17}$  is a straight, branched or cyclic alkyl group having 1 to 6 carbon atoms; and  
15 A is an oxygen atom or a nitrogen atom having a single hydrogen atom bound thereto] with an alkyl halide represented by the following general formula (13):

[Chemical Formula 13]



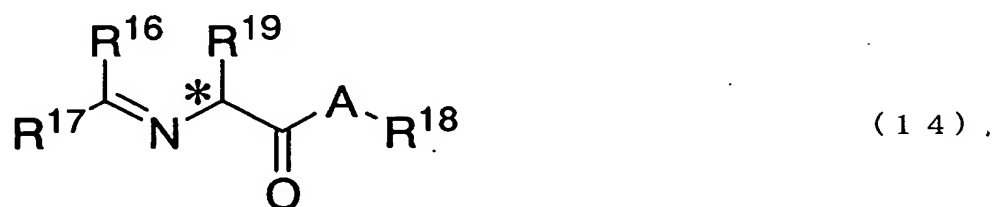
20 [wherein  $\text{R}^{18}$  is a straight, branched or cyclic alkyl group having 1 to 10 carbon atoms, a straight, branched or cyclic



alkenyl group having 3 to 10 carbon atoms, a straight,  
 branched or cyclic alkynyl group having 3 to 10 carbon atoms,  
 or an aralkyl group that has 5 to 25 carbon atoms and may or  
 may not have its nucleus substituted with 1 to 15 halogen

atoms; and Y is a chlorine atom, a bromine atom, or an iodine  
 atom], comprising reacting, in a two-phase solution, a Schiff  
 base of a glycine ester or an amide, then the following  
 general formula (14),

[Chemical Formula 14]



[wherein R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup> and A are as defined above, and the  
 chiral carbon indicated by an asterisk '\*' has an absolute  
 configuration of (R) or (S)], that is a method for producing  
 the chemical compound represented in the above general formula  
 (14).

[Claim 31] The method for carrying out a reaction wherein  
 the ammonium salt according to claims 1 to 4, represented by  
 the general formula above (1) is used as intermediate transfer  
 catalysis in a three-phase solution comprising an organic  
 solvent with hydrogen atoms substituted with fluorine atoms,  
 an organic solvent, and water.

[Claim 32] The method according to claim 30, wherein the

reaction is carried out in a three-phase solution comprising an organic solvent with hydrogen atoms substituted with fluorine atoms, an organic solvent, and water.

[Claim 33] A method for recovering and/or purifying an ammonium salt, characterized in that an organic solvent, water, a mixed solvent of an organic solvent and water, and/or an organic solvent with hydrogen atoms substituted with fluorine atoms are/is used to separate the ammonium salt according to any of claims 1 to 4 represented by the above general formula (1) from a product containing the ammonium salt.

[Claim 34] A method for recovering a ammonium salt according to any of claims 1 to 4 represented by the above general formula above (1), characterized in that, following the production of the compound of the above general formula (14) by the method according to claim 30, the ammonium salt is separated from the reaction mixture containing the ammonium salt by using an organic solvent, water, a mixed solvent of an organic solvent and water, and/or an organic solvent with hydrogen atoms substituted with fluorine atoms.

[Claim 35] A method for recovering a ammonium salt according to any of claims 1 to 4 represented by the above general formula (1), characterized in that, following the production of the compound of the above general formula (14) by the method according to claim 30, the ammonium salt is separated from the reaction mixture containing the ammonium

salt by using hexane, water, a mixed solvent of an organic solvent and water, and/or an organic solvent with hydrogen atoms substituted with fluorine atoms.

[Claim 36] A method for reusing a ammonium salt according to claim 1 to 4 represented by the general formula (1) and which is recovered by the method according to claims 34 to 35 as a chiral catalyst for producing the chemical compound according to claim 30 represented by the above general formula (14).

10 [DETAILED DESCRIPTION OF THE INVENTION]

[0001]

[TECHNICAL FIELD TO WHICH THE INVENTION PERTAINS]

The present invention relates to a optically active quaternary ammonium salt and a production method thereof, as well as to a method for recovering and purifying the ammonium salt. The present invention also relates to a method for recovering and purifying a fluorine-containing optically active chemical compound by using an organic solvent with hydrogen atoms substituted with fluorine atoms (i.e., fluorous solvent). The present invention further relates to a method for stereoselectively producing an optically active  $\alpha$ -amino acid derivative, a useful intermediate for the synthesis of pharmaceutical or agrochemical products, by using the ammonium salt as a phase transfer catalyst.

25 [0002]

[PRIOR ART]

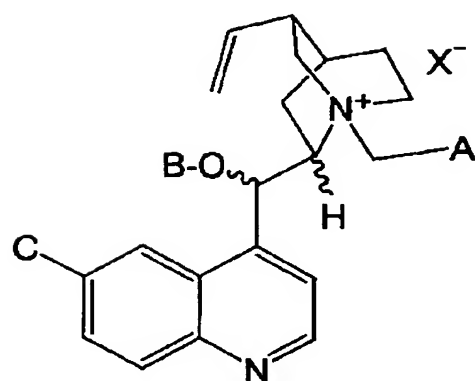
When optically active quaternary ammonium salts are used as phase-transfer catalysts in the production of optically active  $\alpha$ -amino acid derivatives, the catalysts may be recovered afterwards for recycle. In one technique, this is done by neutralizing the aqueous phase with an acid after separation, extracting the aqueous phase with an organic solvent, and then purifying the extract by silica gel column chromatography (Non-Patent Article No. 1). While this technique is advantageous in that the activity of the recycled catalysts is retained, the recovery of the catalyst is only 72% and the technique involves many steps. For this reason, improvement in the recovery of the catalyst is required. Also, the process for recovering catalysts must be simplified enough to be used in industrial applications.

[0003]

A much simpler approach to recover catalysts involves the use of a compound represented by the following formula (15):

[0004]

[Chemical Formula 15]



( 15 )

This compound comprises an ammonium salt derivative of an optically active alkaloid (e.g., quinine, quinidine, cinchonine, and cinchonidine) bound to a polymer such as polystyrene and polyethylene glycol and is suitable for use as a chiral phase-transfer catalyst in the production of optically active  $\alpha$ -amino acid derivatives (See Non-Patent Articles 2-4 for examples in which the polymer is introduced at the position 'A', Non-Patent Article 3 for an example in which the polymer is introduced at the position 'B', and Non-Patent Article No. 5 for an example in which the polymer is introduced at the position 'C'). However, introduction of the polymer moiety may result in a significant decrease in the selectivity of the catalyst (See, for example, Non-Patent Article No. 5). Even many of the catalysts that retain high stereoselectivity of 90% ee or above have not been shown to retain the catalytic performance when recycled following recovery (See, for example, Non-Patent Articles 3 and 4). Although no data is presented, only one example of practically

recyclable catalysts is reported. In this case, a significant reduction of the selectivity is also experienced in this example when a different substrate is used (See, for example, Non-Patent Article No. 2).

5 [0005]

As optically active quaternary ammonium salts in which the backbone structure contains a fluorine atom as a C-F bond, alkaloid derivatives incorporating a fluorine-substituted benzyl group are known (See, for example, Non-Patent Articles  
10 6 and 7). Also, optically active ammonium catalysts having such substituents as a 4-fluorophenyl group and a 3,4,5-trifluorophenyl group (See, for example, Non-Patent Article No. 8), a 3,5-bis(trifluoromethyl)phenyl group or a 3,5-bis{3,5-bis(trifluoromethyl)phenyl}phenyl group (See, for example,  
15 Non-Patent Article No. 9) are known as optically active quaternary ammonium salt derivatives having a chiral axis originating from binaphthyl.

[0006]

Different perfluoro alkyl-containing optically active  
20 asymmetric catalyst ligands are known, including axially chiral binaphthol derivatives (Non-Patent Articles No. 10-14), optically active salen derivatives (See, for example, Non-Patent Articles No. 15-18), optically active ephedrine derivatives (Non-Patent Article No. 19), and optically active  
25 aminothiulates (Non-Patent Article No. 20). Each of these

compounds is used in the synthesis of optically active compounds different from the compounds of the present invention. Attempts for recovery and recycle have been made for some of the compounds. However, except for the asymmetric  
5 protonation agents used in stoichiometric amounts (Non-Patent Article 10), each compound has to be catalytically prepared through the formation of oxygen-metal bonds or complexes: No optically active organic catalysts are known that themselves serve as an asymmetric catalyst. In particular, no optically  
10 active quaternary ammonium salts are known that contain perfluoro alkyl groups consisting of two or more carbon atoms. Nor are any examples known of the use of the salts as asymmetric catalysts or as phase-transfer catalysts. No examples are known in which the phase transfer catalytic  
15 reaction is carried out in a three-phase system consisting of organic, aqueous and fluorous phases, nor are any examples described of the use of fluorous solvents to separate/purify the salts or to recover only the catalyst from the catalyst-containing mixture remaining after the reaction. No examples  
20 are known of recovering the salts to serve as catalysts in a substantially quantitative manner, nor are any examples known in which the salts are recovered in a separate phase of a fluorous solvent and the recovered salts are recycled as an asymmetric catalyst in the same reaction, and which  
25 demonstrate that the performance of the catalyst as measured

by the reactivity and stereoselectivity are retained.

[0007]

[Non-Patent Article No. 1]

K. Maruoka et. al., Tetrahedron Lett. 2000, 41, 8339-8342

5 [Non-Patent Article No. 2]

R. Chinchilla et. al., Tetrahedron: Asymm., 2000, 11,

3277-3281

[Non-Patent Article No. 3]

D. Cahard et. al., Synthesis, 2001, 11, 1742-1746

10 [Non-Patent Article No. 4]

D. Cahard et. al., Tetrahedron: Asymm., 2001, 12, 983-986

[Non-Patent Article No. 5]

M. Benaglia et. al., Tetrahedron: Asymm., 2003, 14, 461-

467

15 [Non-Patent Article No. 6]

H. G. Park et. al., Org. Lett., 2002, Vol. 4, No. 24,

4245-4248

[Non-Patent Article No. 7]

B. R. Cho et. al., J. Org. Chem., 1987, 52, 4752-4756

20 [Non-Patent Article No. 8]

Keiji Maruoka et. al., J. Am. Chem. Soc., 2003, 125,

5139-5151

[Non-Patent Article No. 9]

K. Maruoka et. al., J. Am. Chem. Soc., 2003, 125, 2054-

25 2055



[Non-Patent Article No. 10]

S. Takeuchi et. al., Tetrahedron, 2000, 56, 351-356

[Non-Patent Article No. 11]

S. Takeuchi et. al., Tetrahedron, 2002, 58, 3963-3969

5 [Non-Patent Article No. 12]

K. S. Chan et. al., Tetrahedron, 2002, 58, 3951-3961

[Non-Patent Article No. 13]

D. Sinou et. al., Tetrahedron: Asymm., 2002, 13, 1449-  
1456

10 [Non-Patent Article No. 14]

D. Sinou et. al., Chem. Commun., 2001, 1220-1221

[Non-Patent Article No. 15]

D. Sinou et. al., Tetrahedron, 2002, 58, 3971-3976

[Non-Patent Article No. 16]

15 G. Pozzi et. al., Eur. J. Org. Chem., 1999, 1947-1955

[Non-Patent Article No. 17]

G. Pozzi et. al., Chem. Commun., 2000, 2171-2172

[Non-Patent Article No. 18]

G. Pozzi et. al., Tetrahedron, 2002, 58, 3943-3949

20 [Non-Patent Article No. 19]

S. Takeuchi et. al., Tetrahedron, 2001, 57, 5565-5571

[Non-Patent Article No. 20]

G. v. Koten et. al., Org. Lett., 1999, Vol. 1, No. 6,  
853-855

25 [0008]

[PROBLEM TO BE SOLVED BY THE INVENTION]

In view of the above-described state of the background art, objects of the present invention are:

- 1) to provide a novel optically active quaternary ammonium  
5 salt, that when used as a phase-transfer catalyst in the asymmetric alkylation of a glycine derivative, gives a high stereoselectivity of 90% ee or above and is readily recovered after the reaction;
- 2) to provide the salt that retains its catalytic performance  
10 when recycled;
- 3) to provide a method for readily recovering, separating, and purifying the salt at high yield after the reaction;
- 4) to provide a method for producing the salt;
- 5) to provide a method for using the salt as a phase-transfer  
15 catalyst and thus stereoselectively producing an optically active  $\alpha$ -amino acid derivative suitable for use as an intermediate in the synthesis of pharmaceutical or agrochemical products; and
- 6) to recover the salt used in the reaction and ensure that  
20 high catalytic performance is retained in the recycled salt.

[0009]

[MEANS FOR SOLVING THE PROBLEMS]

In a further effort to address the objects above, it has been found that a novel axially chiral, optically active  
25 ammonium salt that includes a perfluoro group, which is at

least one of substitution group, with hydrogen atoms substituted with fluorine atoms, and such an ammonium salt, after use as a chiral phase-transfer catalyst, can be extracted for recycle with a fluorous solvent that has all hydrogen atoms substituted with fluorine atoms. It is these findings that led to the present invention.

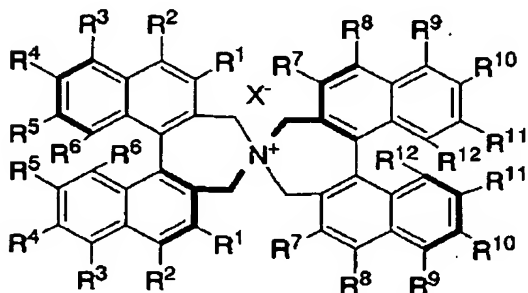
[0010]

Accordingly, the present invention concerns:

1) An optically active quaternary ammonium salt represented by the following general formula (1):

[0011]

[Chemical Formula 16]



[wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ , and  $R^{12}$  are each independently a hydrogen atom, a halogen atom, a methyl group that may or may not be substituted with fluorine, an ethyl group that may or may not be substituted with fluorine, a straight, branched or cyclic alkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic heteroalkyl group that has 3 to 18 carbon atoms and may or may not be substituted with

fluorine, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and may or may not be

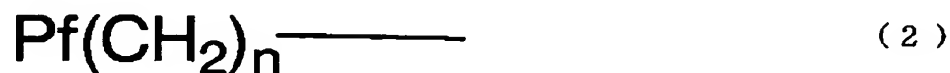
5 substituted with fluorine, an alkoxyl group that has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and may or may not be substituted with fluorine, an aralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with

10 fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine;

with the proviso that at least one of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ , and  $R^{12}$  is a substituent represented by the following general formula (2):

15 [0012]

[Chemical Formula 17]



(wherein Pf is a straight, branched or cyclic alkyl group that has 2 to 18 carbon atoms and has all the hydrogen atoms

20 substituted with fluorine atoms, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms,

an aryl group that has 5 to 20 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, an aralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms, or a heteroaralkyl group that has 5 to 25 carbon atoms and has all the hydrogen atoms substituted with fluorine atoms. n is an integer from 0 to 4.), and/or by the following general formula (3):

[0013]

[Chemical Formula 18]



(wherein Pf and n are as defined in the above general formula (2), R<sup>13</sup> and R<sup>14</sup> are each independently a methyl group, an ethyl group, a vinyl group, a straight, branched or cyclic alkyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 18 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 18 carbon atoms, an alkoxy group having 1 to 18 carbon atoms, an aryl group having 5 to 20 carbon atoms, an aralkyl group having 5 to 25 carbon atoms, a heteroaralkyl group having 5 to 25 carbon atoms, or the general formula above (2)); X<sup>-</sup> is a fluoride ion, a chloride ion, a bromide ion, an iodide ion, a p-toluenesulfonic acid ion, a hydroxide ion, a thiocyanate ion,

a hydrogen sulfate ion, a perchloric acid ion, or a hexafluorophosphoric acid ion; and the two binaphthyl moieties each have a chiral axis so that the absolute configurations of the two binaphthyl moieties are (R, R) or (S, S)].

5 2) The chemical compound, wherein  $R^1$  and  $R^7$ ,  $R^3$  and  $R^9$ ,  $R^4$  and  $R^{10}$ ,  $R^5$  and  $R^{11}$ , and  $R^6$  and  $R^{12}$  in the above general formula (1) are in each case identical to one another;  $R^2$  and  $R^8$  are identical to one another and are each represented by the above general formula (3); and  $X^-$  is a fluorine ion, a chloride ion,  
10 a bromide ion, an iodide ion, a p-toluenesulfonic acid ion, a thiocyanate ion, a hydrogen sulfate ion, or a hydroxide ion.

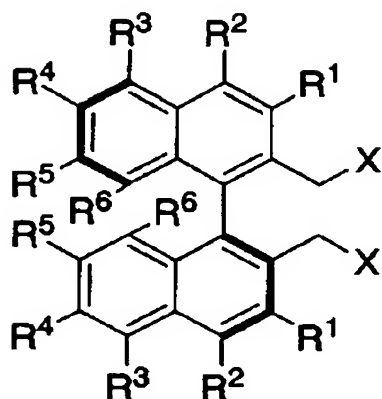
3) The chemical compound, wherein  $R^1$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^9$ ,  $R^{11}$ , and  $R^{12}$  in the above general formula (1) are each independently a hydrogen atom;  $R^2$ ,  $R^4$ ,  $R^8$ , and  $R^{10}$  are identical to one  
15 another and are each represented by the above general formula above (3); and  $X^-$  is a chloride ion, a bromide ion, an iodide ion, or a p-toluenesulfonic acid ion.

4) The chemical component wherein in the general formula above (3),  $n$  is 2,  $R^{13}$  and  $R^{14}$  are each a methyl group, and Pf is an  
20 n-octyl group having all the hydrogen atoms substituted with fluorine atoms, and  $X^-$  is a bromide ion.

5) An optically active binaphthyl compound represented by the following general formula (4):

[0014]

25 [Chemical Formula 19]



( 4 )

[wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are each independently a hydrogen atom, a halogen atom, a methyl group that may or may not be substituted with fluorine, an ethyl group that may or may not be substituted with fluorine, a straight, branched or cyclic alkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic heteroalkyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkenyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, a straight, branched or cyclic alkynyl group that has 3 to 18 carbon atoms and may or may not be substituted with fluorine, an alkoxy group that has 1 to 18 carbon atoms and may or may not be substituted with fluorine, an aryl group that has 5 to 20 carbon atoms and may or may not be substituted with fluorine, an aralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with fluorine, or a heteroaralkyl group that has 5 to 35 carbon atoms and may or may not be substituted with

fluorine; with the proviso that at least one of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , and  $R^6$  is a substituent represented by the general formula above (2) or general formula above (3): X is a chlorine atom, a bromine atom, an iodine atom, or a p-toluenesulfonyloxy

group; and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S)].

6) The chemical compound wherein  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  in the above general formula (3) are each independently a hydrogen atom; and  $R^2$  and  $R^4$  are identical to one another and are each

represented by the above general formula (3).

[0015]

7) The chemical compound according to 6), wherein in the above general formula (3), n is 2,  $R^{13}$  and  $R^{14}$  are each a methyl group, and Pf is an n-octyl group having all the hydrogen atoms

substituted with fluorine atoms, and X is a bromine atom.

8) A method for producing the chemical compound according to any of 1) to 4) above represented by the above general formula (1) in which  $X^-$  is a chloride ion, a bromide ion, an iodide ion, or a p-toluenesulfonic acid ion, characterized in that the

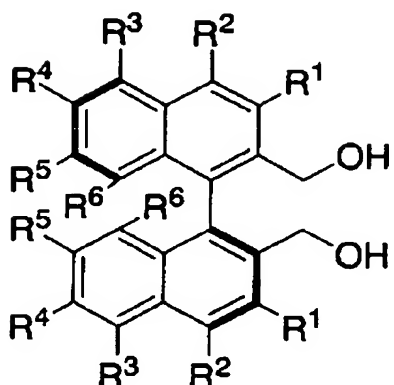
chemical compound according to any of 5) to 7) above represented by the above general formula (4) is reacted with ammonia.

9) An optically active binaphthyl dihydroxyl compound represented by the following general formula (5):

[0016]



[Chemical Formula 20]



( 5 )

(wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , and  $R^6$  are each as defined

according to 5) above in the general formula above (4), and

5 the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S))

10) The chemical compound according to 9), wherein in the

above general formula (5),  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each

independently a hydrogen atom, and  $R^2$  and  $R^4$  are identical to

10 one another and are each represented by the above general formula (3).

11) The chemical compound according to 10), wherein in the

above general formula (3),  $n$  is 2,  $R^{13}$  and  $R^{14}$  are each a methyl

group, and Pf is an  $n$ -octyl group having all the hydrogen

15 atoms substituted with fluorine atoms.

12) A method for producing the chemical compound of the

general formula above (3) according to any of 5) to 7),

characterized in that the chemical compound of the above

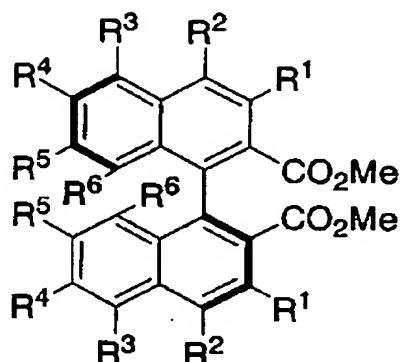
general formula (5) according to any of 9) to 11) is reacted

20 with a halogen source or  $p$ -toluenesulfonyl chloride.

13) An optically active binaphthyl diester compound represented by the following general formula (6) :

[0017]

[Chemical Formula 21]



( 6 )

5

(wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , and  $R^6$  are each as defined according to 5) above in the general formula above (4), and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S))

10 14) The chemical compound according to 13), wherein in the above general formula (6),  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each independently a hydrogen atom, and  $R^2$  and  $R^4$  are identical to one another and are each represented by the above general formula (3);

15 15) The chemical compound according to 14) above, wherein in the above general formula (3),  $n$  is 2,  $R^{13}$  and  $R^{14}$  are each a methyl group, and Pf is an  $n$ -octyl group having all the hydrogen atoms substituted with fluorine atoms.

16) A method for producing the chemical compound according to  
20 any of 9) to 11) above represented by the general formula

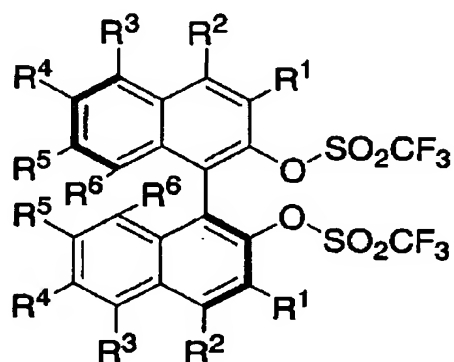
above (5), characterized in that the chemical compound according to any of 13) to 15) above represented by the general formula above (6) is reacted with a hydrogen anion.

17) An optically active binaphthyl compound represented by the

5 following general formula (7):

[0018]

[Chemical Formula 22]



(7)

(wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, and R<sup>6</sup> are each as defined

10 according to 5) above in the general formula above (4), and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S))

18) The chemical compound according to 17), wherein in the above general formula (7), R<sup>1</sup>, R<sup>3</sup>, R<sup>5</sup>, and R<sup>6</sup> are each

15 independently a hydrogen atom, and R<sup>2</sup> and R<sup>4</sup> are identical to one another and are each represented by the above general formula (3);

19) The chemical compound according to 18), in the above general formula (3), n is 2, R<sup>13</sup> and R<sup>14</sup> are each a methyl group,

20 and Pf is an n-octyl group having all the hydrogen atoms

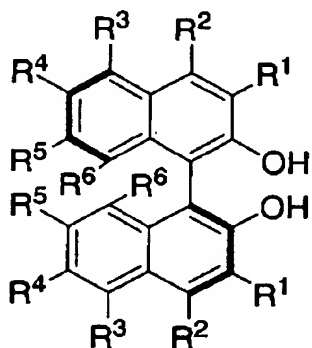
substituted with fluorine atoms.

20) A method for producing the chemical compound of the general formula above (6) according to any of 13) to 15), characterized in that the chemical compound of the general formula above (7) according to any of 17) to 19) is reacted with carbon monoxide and methanol in the presence of a palladium catalyst and an organic base.

21) An optically active binaphthol compound represented by the following general formula (8):

[0019]

[Chemical Formula 23]



( 8 )

(wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , and  $R^6$  are each as defined according to 5) above in the general formula above (4), and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S))

22) The chemical compound according to 21), wherein in the above general formula (8),  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each independently a hydrogen atom, and  $R^2$  and  $R^4$  are identical to one another and are each represented by the above general

formula (3).

23) The chemical compound according to 22), wherein in the above general formula (3),  $n$  is 2,  $R^{13}$  and  $R^{14}$  are each a methyl group, and Pf is an  $n$ -octyl group having all the hydrogen

5 atoms substituted with fluorine atoms.

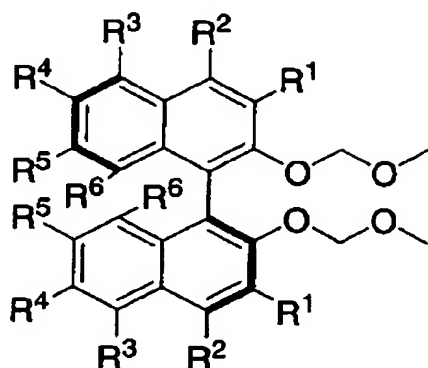
24) A method for producing the chemical compound according to any of 17) to 19) above represented by the above general formula (7), characterized in that the chemical compound

10 according to any of 21) to 23) above represented by the above general formula (8) is reacted with a triflating agent.

25) An optically active binaphthyl bis-methoxymethyl ether compound represented by the following general formula (9):

[0020]

[Chemical Formula 24]



( 9 )

15

(wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , and  $R^6$  are each as defined according to 5) above in the general formula above (4), and the binaphthyl moiety has a chiral axis so that the absolute configuration of the binaphthyl moiety is (R) or (S))

20 26) The chemical compound according to 25), wherein in the

above general formula above (9),  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each independently a hydrogen atom, and  $R^2$  and  $R^4$  are identical to one another and are each represented by the above general formula (3).

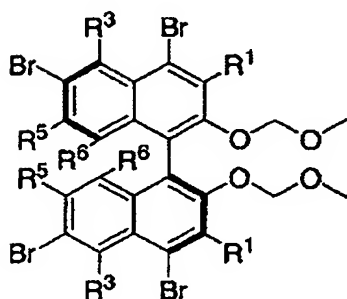
27) The chemical compound according to 26), wherein in the general formula above (3),  $n$  is 2,  $R^{13}$  and  $R^{14}$  are each a methyl group, and Pf is an  $n$ -octyl group having all the hydrogen atoms substituted with fluorine atoms.

28) A method for producing the chemical compound according to any of 21) to 23) represented by the above general formula (8), characterized in that the chemical compound according to any of 25) to 27 represented by the above general formula (9) is reacted with an acid.

29) An optically active binaphthyl bis-methoxymethyl ether compound represented by the following general formula (10):

[0021]

[Chemical Formula 25]



(10)

[wherein  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each as defined according to 5) above in the general formula above (4), and the binaphthyl moiety has a chiral axis so that the absolute configuration of

the binaphthyl moiety is (R) or (S)], comprising reacting with an alkyl lithium the chemical compound, and the following general formula (11)

[0022]

5 [Chemical Formula 26]



[wherein  $\text{R}^{13}$ ,  $\text{R}^{14}$ , Pf, and n are each as defined in the general formula above (3)] and subsequently reacting with the reaction product according to 25) to 27) represented by the above

10 general formula (9).

30) In the presence of the chemical compound according to 1) to 4) represented by the general formula (1) and an inorganic base, the following general formula (12)

[0023]

15 [Chemical Formula 27]



[wherein  $\text{R}^{15}$  and  $\text{R}^{16}$  are each independently a hydrogen atom or an aryl group that has 5 to 10 carbon atoms and may or may not be substituted with halogen, with the proviso that  $\text{R}^{15}$  and  $\text{R}^{16}$

20 are not a hydrogen atom at the same time;  $\text{R}^{17}$  is a straight, branched or cyclic alkyl group having 1 to 6 carbon atoms; and

A is an oxygen atom or a nitrogen atom having a single hydrogen atom bound thereto] with an alkyl halide represented by the following general formula (13):

[0024]

5 [Chemical Formula 28]



[wherein  $\text{R}^{18}$  is a straight, branched or cyclic alkyl group having 1 to 10 carbon atoms, a straight, branched or cyclic alkenyl group having 3 to 10 carbon atoms, a straight, branched or cyclic alkynyl group having 3 to 10 carbon atoms, or an aralkyl group that has 5 to 25 carbon atoms and may or may not have its nucleus substituted with 1 to 15 halogen atoms; and Y is a chlorine atom, a bromine atom, or an iodine atom] comprising reacting, in a two-phase solution, a Schiff base of a glycine ester or an amide represented by the following general formula (14):

[0025]

[Chemical Formula 29]



20 [wherein  $\text{R}^{15}$ ,  $\text{R}^{16}$ ,  $\text{R}^{17}$ ,  $\text{R}^{18}$  and A are as defined above, and the chiral carbon indicated by an asterisk '\*' has an absolute



configuration of (R) or (S)], that is a method for stereoselectively producing the chemical compound in the general formula (14).

31) The method for carrying out a reaction wherein the ammonium salt according to 1) to 4), represented by the above general formula (1) is used as intermediate transfer catalysis in a three-phase solution comprising an organic solvent with hydrogen atoms substituted with fluorine atoms, an organic solvent, and water.

32) The method according to claim 29), wherein the reaction is carried out in a three-phase solution comprising an organic solvent with hydrogen atoms substituted with fluorine atoms, an organic solvent, and water

33) A method for recovering and/or purifying an ammonium salt, characterized in that an organic solvent, water, a mixed solvent of an organic solvent and water, and/or an organic solvent with hydrogen atoms substituted with fluorine atoms are/is used to separate the ammonium salt according to any of claims 1) to 4) represented by the above general formula (1) from a product containing the ammonium salt.

34) A method for recovering a ammonium salt according to any of claims 1) to 4) represented by the above general formula (1) , characterized in that, following the production of the compound of the above general formula (14) by the method according to 30), the ammonium salt is separated from the

reaction mixture containing the ammonium salt by using an organic solvent, water, a mixed solvent of an organic solvent and water, and/or an organic solvent with hydrogen atoms substituted with fluorine atoms.

5 35) A method for recovering a ammonium salt according to any of claims 1) to 4) represented by the above general formula above (1), characterized in that, following the production of the compound of the above general formula (14) by the method according to 30), the ammonium salt is separated from the  
10 reaction mixture containing the ammonium salt by using hexane, water, a mixed solvent of an organic solvent and water, and/or an organic solvent with hydrogen atoms substituted with fluorine atoms.

36) A method for reusing a ammonium salt according to claim 1  
15 to 4 represented by the general formula (1) and which is recovered by the method according to 34) to 35) as a chiral catalyst for producing the chemical compound according to 30) represented by the above general formula (14).

[0026]

20 The present invention will now be described in detail.

[0027]

While the optically active quaternary ammonium salt of the present invention shown by the above general formula (1) may be any of the compounds defined above, it preferably is a  
25 compound in which  $R^1$  and  $R^7$ ,  $R^3$  and  $R^9$ ,  $R^4$  and  $R^{10}$ ,  $R^5$  and  $R^{11}$ ,

and  $R^6$  and  $R^{12}$  are in each case identical to one another,  $R^2$  and  $R^8$  are identical to one another and are each represented by the general formula (3), and  $X^-$  is a fluoride ion, a chloride ion, a bromide ion, an iodide ion, a p-toluenesulfonic acid ion, or a hydroxide ion. Of such compounds, particularly preferred are those in which  $R^1$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^9$ ,  $R^{11}$ , and  $R^{12}$  are each a hydrogen atom,  $R^2$ ,  $R^4$ ,  $R^8$ , and  $R^{10}$  are identical to one another and are each represented by the general formula (3), and  $X^-$  is a chloride ion, a bromide ion, an iodide ion, or a p-toluenesulfonic acid ion. Of these, the most preferred are those in which  $R^{13}$  and  $R^{14}$  in the general formula above (3) are a substituent selected from the group consisting of a methyl group, Pf is a n-octyl group that has all the hydrogen atoms substituted with fluorine atoms, n is 2, and  $X^-$  is a bromide ion.

[0028]

Examples of the compound shown by the above general formula (1) include, specifically, spiro-bis{(R)-1,1'-bi-[4-(2-perfluorooctylethyl)dimethylsilyl]naphthyl-2,2'-dimethyl}ammonium bromide, spiro-bis{(R)-1,1'-bi-[6-(2-perfluorooctylethyl)dimethylsilyl]naphthyl-2,2'-dimethyl}ammonium bromide, spiro-bis{(R)-1,1'-bi-[4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-perfluorooctyl)ethyl]naphthyl-2,2'-dimethyl}ammonium bromide, spiro-bis{(R)-1,1'-bi-[4,6-bis((2-

perfluorooctylethyl)dimethylsilyl)naphthyl-2,2'-  
dimethyl}ammonium bromide, spiro-bis{(R)-1,1'-bi-[4,6-bis(-  
tris(2-perfluorooctylethyl)silyl)naphthyl-2,2'-  
dimethyl}ammonium bromide, spiro-bis{(R)-1,1'-bi-[4,6-bis((2-  
5 perfluorooctylethyl)dimethylsilyl)naphthyl-2,2'-  
dimethyl}ammonium fluoride, spiro-bis{(R)-1,1'-bi-[4,6-bis((2-  
perfluorooctylethyl)dimethylsilyl)naphthyl-2,2'-  
dimethyl}ammonium chloride, spiro-bis{(R)-1,1'-bi-[4,6-bis((2-  
perfluorooctylethyl)dimethylsilyl)naphthyl-2,2'-  
10 dimethyl}ammonium iodide, spiro-bis{(R)-1,1'-bi-[4,6-bis((2-  
perfluorooctylethyl)dimethylsilyl)naphthyl-2,2'-  
dimethyl}ammonium hydroxide, and spiro-bis{(R)-1,1'-bi-[4,6-  
bis((2-perfluorooctylethyl)dimethylsilyl)naphthyl-2,2'-  
dimethyl}ammonium-4-methylbenzene sulfonate, and the  
15 corresponding (S)-forms as enantiomers.

[0029]

The optically active binaphthyl compound of the present  
invention shown by the above general formula (4) is preferably  
such that  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each a hydrogen atom, and  $R^2$   
20 and  $R^4$  are identical to one another and are each represented by  
the above general formula (3). Of such compounds, the most  
preferred are those in which  $R^{13}$  and  $R^{14}$  are each a methyl group,  
and Pf is an n-octyl group having all the hydrogen atoms  
substituted with fluorine atoms, n is 2, and  $X^-$  is a bromide  
25 ion in the above general formula above (3).

[0030]

Examples of the optically active binaphthyl compound of the present invention shown by the above general formula (4) include, (R)-1,1'-bi-{2-bromomethyl-4-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-bromomethyl-6-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-bromomethyl-4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-perfluorooctyl)ethyl}naphthyl, (R)-1,1'-bi-{2-bromomethyl-4,6-bis((2-perfluorooctylethyl)dimethylsilyl)}naphthyl, (R)-1,1'-bi-{2-bromomethyl-4,6-bis[-tris(2-perfluorooctylethyl)silyl]}naphthyl, (R)-1,1'-bi-{2-chloromethyl-4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]}naphthyl, (R)-1,1'-bi-{2-iodomethyl-4,6-bis((2-perfluorooctylethyl)dimethylsilyl)}naphthyl and (R)-1,1'-bi-{2-(4-methylbenzenesulfonyloxy)methyl-4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]}naphthyl, and the corresponding (S)-forms as enantiomers.

20 [0031]

The compound of the present invention represented by the above general formula (1) can be obtained by reacting the optically active binaphthyl compound of the above general formula (4) with ammonia. The ammonia used may be a 10% to saturated aqueous ammonia and preferably a 20 to 28wt% aqueous

ammonia. Water or an organic solvent inert to the reaction may be added as a solvent. The reaction is preferably carried out in a sealed condition to avoid loss of ammonia. The amount of ammonia used is typically 1 to 8 equivalents, and preferably 2  
5 to 5 equivalents, relative to the substrate used. The reaction is typically carried out at a temperature of 5°C to 30°C and at a substrate concentration of 5 to 20wt%, and is carried out over a time period of typically 5 to 72 hours, and preferably 10 to 36 hours. In this manner, the desired ammonium salt can  
10 be obtained in high yield.

[0032]

While the optically active binaphthyl dihydroxy compound of the present invention shown by the above general formula (5), it preferably is a compound in which R<sup>1</sup>, R<sup>3</sup>, R<sup>5</sup>, and R<sup>6</sup> are  
15 each a hydrogen atom, and R<sup>2</sup> and R<sup>4</sup> are identical to one another and are each represented by the general formula (3). Of these, the most preferred are those in which R<sup>13</sup> and R<sup>14</sup> are each a methyl group, and Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms, and n is 2 in  
20 the above general formula (3)

[0033]

Examples of the optically active binaphthyl diester compound of the present invention shown by the above general formula (5) include, (R)-1,1'-bi-{2-methoxycarbonyl-4-(2-  
25 perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-

methoxycarbonyl-6-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-methoxycarbonyl-4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-perfluorooctyl)ethyl}naphthyl, (R)-1,1'-bi-{2-methoxycarbonyl-4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]}naphthyl and (R)-1,1'-bi-{2-methoxycarbonyl-4,6-bis[-tris(2-perfluorooctylethyl)silyl]}naphthyl, and the corresponding (S)-forms as enantiomers.

[0034]

10 When it is desired to produce a optically active binaphthyl dihalogen compound of the present invention represented by the above general formula (4), for example, it can be obtained by reacting the optically active binaphthyl dihydroxyl compound of the above general formula (5) with  
15 triphenylphosphine and Tetrabromomethane or carbon tetrachloride and the like in a proper solvent such as tetrahydrofuran. The reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically -10°C to 50°C , and preferably 10°C to 30°C, and is  
20 carried out over a time period of typically 1 hour to 5 hours. In this manner, the desired dihalogen product can be obtained in high yield.

[0035]

When it is desired to produce a optically active  
25 binaphthyl sulfonate compound of the present invention

represented by the above general formula (4), for example, it can be obtained by reacting the optically active binaphthyl dihydroxyl compound of the above general formula (5) with p-toluenesulfonyl chloride in a proper solvent such as

5 dichloromethane in the presence of an acid-capturing agent such as triethylamine. The reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically -40°C to 20°C, and preferably -10°C to 10°C, and is carried out over a time period of typically 1 hour to 5 hours.  
10 In this manner, the desired sulfonyloxy product can be obtained in high yield.

[0036]

The optically active binaphthyl diester compound of the present invention shown by the above general formula (6) is  
15 preferably such that  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each a hydrogen atom, and  $R^2$  and  $R^4$  are identical to one another and are each represented by the above general formula (3). Of such compounds, the most preferred are those in which  $R^{13}$  and  $R^{14}$  are each a methyl group, and Pf is an n-octyl group having all the  
20 hydrogen atoms substituted with fluorine atoms, and n is 2 in the above general formula (3).

[0037]

Examples of the optically active binaphthyl diester compound of the present invention shown by the formula (6)  
25 include, (R)-1,1'-bi-{2-methoxycarbonyl-4-(2-



perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-methoxycarbonyl-6-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-methoxycarbonyl-4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-perfluorooctyl)ethyl}naphthyl, (R)-1,1'-bi-{2-methoxycarbonyl-4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]}naphthyl and (R)-1,1'-bi-{2-methoxycarbonyl-4,6-bis[-tris(2-perfluorooctylethyl)silyl]}naphthyl, and the corresponding (S)-forms as enantiomers.

10 [0038]

The optically active binaphthyl dihydroxy compound of the present invention represented by the above general formula (5) can be obtained, for example, by reacting the optically active binaphthyl diester compound of the above general formula above  
15 (6) with a hydrogen anion such as  $\text{LiAlH}_4$  in a proper solvent such as tetrahydrofuran. The reaction is carried out at a substrate concentration of typically 5 to 30wt% and at a temperature of typically  $-20^\circ\text{C}$  to  $30^\circ\text{C}$ , and preferably  $-10^\circ\text{C}$  to  $10^\circ\text{C}$ , and is carried out over a time period of typically 10  
20 minutes to 5 hours, and preferably 20 minutes to 2 hours. In this manner, the desired dihydroxyl methyl product can be obtained in high yield.

[0039]

While the optically active binaphthyl compound of the  
25 present invention shown by the above general formula (7), it

preferably is a compound in which  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each a hydrogen atom, and  $R^2$  and  $R^4$  are identical to one another and are each represented by the general formula (3). Of these, the most preferred are those in which  $R^{13}$  and  $R^{14}$  are each a methyl group, and Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms, and n is 2 in the above general formula above (3).

[0040]

Examples of the optically active binaphthyl compound of the present invention shown by the above general formula (7) include (R)-1,1'-bi-{4-(2-perfluorooctylethyl)dimethylsilyl-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{6-(2-perfluorooctylethyl)dimethylsilyl-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-perfluorooctyl)ethyl-2-trifluoromethanesulfonyl}naphthyl, (R)-1,1'-bi-{4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]-2-trifluoromethanesulfonyl}naphthyl and (R)-1,1'-bi-{4,6-bis[tris(2-perfluorooctylethyl)silyl]-2-trifluoromethanesulfonyl}naphthyl, and the corresponding (S)-forms as enantiomers.

[0041]

The optically active binaphthyl dimethyl ester compound of the present invention represented by the above general formula (6) can be obtained, for example, by reacting the

optically active binaphthyl compound of the above general formula (7) with carbon monoxide and methanol in a proper solvent such as dimethyl sulfoxide in the presence of a palladium catalyst and an organic base, such as

5 diisopropylethylamine, for capturing an acid, in a carbon monoxide atmosphere, which may be pressurized. The reaction is carried out at a substrate concentration of typically 5 to 30wt% under a pressure of typically 1 to 30atm, and preferably 5 to 20atm, and at a temperature of typically room temperature

10 to 200°C, and preferably 80°C to 130°C, and is typically carried out over a time period of 24 to 72 hours. The palladium catalyst may have no valency or it may be prepared in the reaction system from a divalent acetate or the like. The palladium catalyst is typically used in an amount of 5 to

15 20mol% relative to the substrate. The base is used in an amount of typically 2 to 8 equivalents, and preferably 2.5 to 5 equivalents, relative to the substrate. Methanol is used in an amount of 2 to 200 equivalents, and preferably 10 to 50 equivalents, relative to the substrate. In this manner, the

20 desired diester product can be obtained in high yield.

[0042]

While the optically active binaphthol compound of the present invention shown by the above general formula (8), it preferably is a compound in which  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each a

25 hydrogen atom, and  $R^2$  and  $R^4$  are identical to one another and

are each represented by the general formula (3). Of such compounds, the most preferred are those in which  $R^{13}$  and  $R^{14}$  are each a methyl group, Pf is an n-octyl group with all the hydrogen atoms substituted with fluorine atoms, and n is 2 in the above general formula above (3).

[0043]

Specific examples of the optically active binaphthol compound of the present invention shown by the above general formula (8) include (R)-1,1'-bi-{2-hydroxy-4-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-hydroxy-6-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-hydroxy-4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-perfluorooctyl)ethyl}naphthyl, (R)-1,1'-bi-{2-hydroxy-4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]}naphthyl and (R)-1,1'-bi-{2-hydroxy-4,6-bis[-tris(2-perfluorooctylethyl)silyl]}naphthyl, and the corresponding (S)-forms as enantiomers.

[0044]

The optically active binaphthyl compound of the present invention represented by the above general formula above (7) can be obtained, for example, by reacting the optically active binaphthol compound of the above general formula (8) with a triflating agent, such as a trifluoromethanesulfonic acid anhydride or trifluoromethanesulfonyl chloride, in an inert solvent such as dichloromethane in the presence of an organic

base such as triethylamine. The reaction is typically carried out at a substrate concentration of 5 to 30wt% and at a temperature of -78°C to room temperature, and is typically carried out over a time period of 30 minutes to 3 hours. In this manner, the desired ditriflate product can be obtained in high yield.

[0045]

The optically active binaphthyl bis-methoxymethyl ether compound of the present invention shown by the above general formula (9) is preferably such that  $R^1$ ,  $R^3$ ,  $R^5$ , and  $R^6$  are each a hydrogen atom, and  $R^2$  and  $R^4$  are identical to one another and are each represented by the general formula (3). Of such compounds, the most preferred are those in which in the above general formula (3),  $R^{13}$  and  $R^{14}$  are each a methyl group, Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms, and n is 2.

[0046]

Examples of the optically active binaphthyl bis-methoxymethyl ether compound of the present invention shown by the above general formula (9) include, (R)-1,1'-bi-{2-methoxymethoxy-4-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-methoxymethoxy-6-(2-perfluorooctylethyl)dimethylsilyl}naphthyl, (R)-1,1'-bi-{2-methoxymethoxy-4-(2-perfluorooctylethyl)dimethylsilyl-6-(2-perfluorooctyl)ethyl}naphthyl, (R)-1,1'-bi-{2-methoxymethoxy-

4,6-bis[(2-perfluorooctylethyl)dimethylsilyl]naphthyl and  
(R)-1,1'-bi-{2-methoxymethoxy-4,6-bis[-tris(2-  
perfluorooctylethyl)silyl]}naphthyl, and the corresponding  
(S)-forms as enantiomers.

5 [0047]

The optically active binaphthol compound of the present  
invention represented by the above general formula (8) can be  
obtained, for example, by reacting the optically active  
binaphthyl bis-methoxymethyl ether compound of the above  
10 general formula (9) with an organic acid, such as p-  
toluenesulfonic acid, in a proper solvent, such as  
dichloromethane and methanol, or a mixed solvent. Preferably,  
the organic acid is used in an amount of 2 to 3 equivalents  
relative to the substrate. The reaction is carried out at a  
15 substrate concentration of typically 5 to 20wt% and at a  
temperature of typically 10°C to 80°C, preferably 30°C to 60°C,  
and is carried out over a time period of typically 20 minutes  
to 48 hours, and preferably 2 hours to 24 hours. In this  
manner, the desired binaphthol product can be obtained in high  
20 yield.

[0048]

The optically active binaphthyl compound of the present  
invention represented by the above general formula (9) can be  
obtained, for example, as follows: The optically active  
25 binaphthyl diether compound of the above general formula (10)

is reacted with butyl lithium in a proper solvent, such as tetrahydrofuran, to replace the bromine atoms with lithium atoms. The reaction product is then reacted with the silyl chloride of the above general formula (11). Using the alkyl  
5 lithium in an amount of typically 8 to 12 equivalents relative to the substrate, the reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically -100°C to -50°C, and preferably -85°C to -75°C, and is carried out over a time period of typically 20 minutes to 3  
10 hours, and preferably 30 minutes to 2 hours. In this manner, the desired lithio product can be obtained. To this product, the alkyl silyl chloride is added, at the same temperature, in an amount of 4 to 8 equivalents relative to the substrate, and the reaction is carried out at a temperature of typically -  
15 80°C to 30°C, and preferably 0°C to room temperature, over a time period of typically 20 minutes to 2 hours, and preferably 30 minutes to 1 hour. In this manner, the desired product can be obtained in high yield.

[0049]

20 While the optically active binaphthyl bis-methoxymethyl ether compound of the present invention shown by the above general formula (10) may be any of the compounds defined above, it preferably is a compound in which R<sup>1</sup>, R<sup>3</sup>, R<sup>5</sup> and R<sup>6</sup> are each a hydrogen atom.

25 [0050]

While the silyl chloride of the present invention shown by the above general formula (11) may be any of the compounds defined above, compounds are the most preferred are those in which in the above general formula (3),  $R^{13}$  and  $R^{14}$  are each a methyl group, Pf is an n-octyl group having all the hydrogen atoms substituted with fluorine atoms, and n is 2.

[0051]

The compound of the present invention represented by the above general formula (10) can be obtained by reacting a corresponding binaphthol product with sodium hydride in a solvent, such as tetrahydrofuran, to form an alkoxide, followed by addition of chloromethylmethyl ether. The reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically -40°C to room temperature, and preferably -10°C to 0°C, and is carried out over a time period of typically 20 minutes to 3 hours, and preferably 30 minutes to 2 hours. In this manner, the desired product can be obtained in high yield.

[0052]

According to the present invention, the optically active quaternary ammonium salt of the above general formula (1) is used as a chiral phase-transfer catalyst. In the stereoselective production of the compound of the above general formula(14), for example, using the optically active quaternary ammonium salt as a phase-transfer catalyst of the



general formula above (1), and a Schiff base of a glycine ester shown by the above general formula (12) is asymmetrically alkylated with a halogenated alkyl of the above general formula (13) in a two-phase solvent system using the  
5 optically active quaternary ammonium salt of the above general formula (1) as a phase-transfer catalyst. The solvent used is a mixture of a water-immiscible hydrocarbon solvent, such as toluene, and a 5 to 60wt% aqueous solution of an alkaline metal, such as potassium hydroxide and cesium hydroxide, with  
10 the ratio of the organic phase to the aqueous phase being in the range of 5:1 to 1:3, preferably, 5:1 to 1:1. This reaction is carried out at a substrate concentration of typically 5 to 20wt% and at a temperature of typically -40°C to 10°C, and preferably -25°C to 5°C, and is carried out over a time period  
15 of typically 1 hour to 200 hours, and preferably 5 hours to 180 hours. The amount of the phase-transfer catalyst used is in the range of 0.5 to 5mol%, and preferably in the range of 2.0 to 4.0mol% relative to the substrate. In this manner, the desired optically active  $\alpha$ -amino acid derivative can be  
20 obtained in high yield in a highly stereoselective manner. In the above-describe process, the reaction product shown by the above general formula (14) is given as an (S)-form when the axially chiral, optically active quaternary ammonium salt of the above general formula (1) to serve as the phase-transfer  
25 catalyst has an absolute configuration of (R, R). Conversely,

the product is given as an (R)-form when the catalyst has an absolute configuration of (S, S).

[0053]

According to the present invention, the above-described  
5 process may be carried out in a three-phase solvent system comprising an organic solvent with the hydrogen atoms substituted with fluorine atoms, an organic solvent and water. The organic solvent with the hydrogen atoms substituted with fluorine atoms may be a fluorous solvent. Examples of fluorous  
10 solvent are perfluorinated alkanes and cycloalkanes, such as perfluorohexane and perfluoromethylcyclohexane. The fluorous solvent is added in an amount of 0.1 to 1.0 times by volume of the organic solvent used.

[0054]

15 The optically active quaternary ammonium salt can be recovered by using any proper technique, may be any of the recovering methods, according to the present invention, it can be recovered after it has been used in the reaction as a catalyst. When necessary, the reaction mixture is diluted with  
20 water and an organic solvent, such as toluene, and is then subjected to separation with a fluorous solvent, such as perfluorinated alkanes and cycloalkanes, including perfluorohexane and perfluoromethylcyclohexane. In this manner, only the catalyst can be recovered from the fluorous layer in  
25 high yield.

[0055]

According to the present invention, the recovered catalyst can be purified by removing the fluorous solvent from the fluorous solution by distillation, and subjecting the  
5 residue to a silica gel column chromatography using a relatively high polar organic solvent, such as a mixed solvent of dichloromethane/methanol, as an eluant. The crude recovered product obtained by concentrating the fluorous solvent may be directly used as a catalyst in the subsequent reaction.

10 [0056]

[Effect of the invention]

According to the present invention,

1) a novel optically active quaternary ammonium salt, that is effective as a phase-transfer catalyst in the asymmetric

15 alkylation of a glycine derivative is provided and,

2) a novel optically active quaternary ammonium salt is easy for readily recovering, producing, and purifying, and it is ensured that high catalytic performance is retained in the recycled salt.

20 [0057]

The present invention is particularly efficient for industry to provide a method for using the novel optically active quaternary ammonium salt as a phase-transfer catalyst and thus stereoselectively producing an optically active  $\alpha$ -  
25 amino acid derivative suitable for use as an intermediate in

the synthesis of pharmaceutical or agrochemical products

[0058]

[Examples]

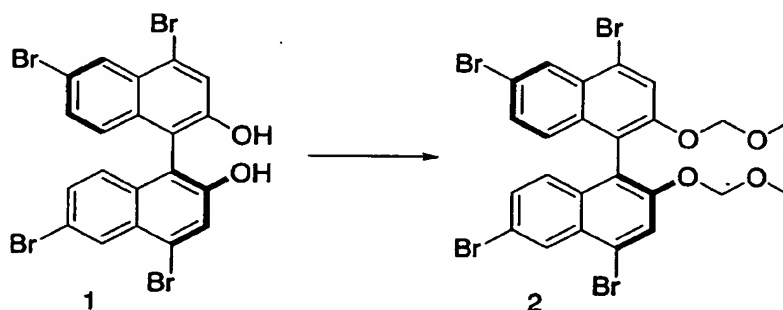
The present invention will now be described in further  
5 detail. These examples, however, are provided by way of  
example only and are not intended to limit the scope of the  
invention in any way.

[0059]

Example 1 Synthesis of (R)-1,1'-bi-(4,6-dibromo-2-  
10 methoxymethoxy)naphthyl (2) (synthesis of precursor)

[0060]

[Chemical Formula 30]



In an argon atmosphere, 60% sodium hydride (0.880 g, 22  
15 mmol) was added to a tetrahydrofuran solution (50 mL) of  
Compound 1 (6.02 g, 10 mmol) at 0°C and the mixture was stirred  
for 10 minutes. Subsequently, chloromethyl ether (1.67 mL, 22  
mmol) was added at 0°C, and the reaction mixture was allowed  
to warm to room temperature and was then stirred for 1 hour.  
20 After completion of the reaction, the reaction mixture was  
poured into water and was extracted with dichloromethane. The

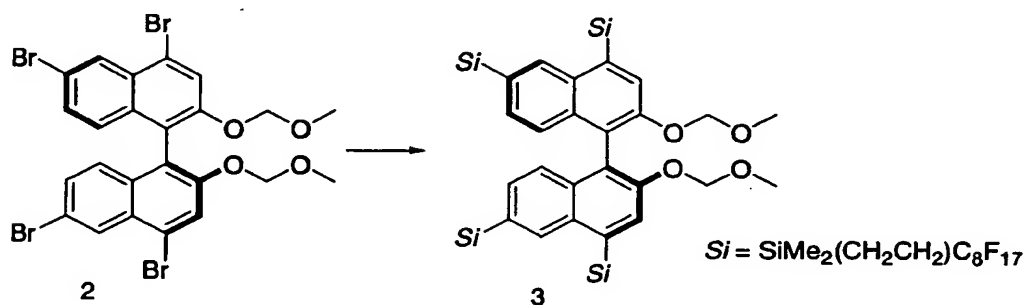
dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. To the resulting white solid, hexane (30 mL) was added and the solution was filtered to give Compound 2 (6.90 g, 10 mmol) in a quantitative manner.

$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\sigma$  8.43 (2H, d,  $J = 2.4$  Hz, Ar-H), 7.94 (2H, s, Ar-H), 7.33 (2H, dd,  $J = 2.4$  Hz, 9.2 Hz, Ar-H), 6.96 (2H, d,  $J = 9.2$  Hz, Ar-H), 5.07 (2H, d,  $J = 7.2$  Hz, Ar- $\text{OCH}_2$ ), 4.98 (2H, d,  $J = 7.2$  Hz, Ar- $\text{OCH}_2$ ), 3.20 (6H, s,  $\text{OCH}_3$ ).

Example 2 Synthesis of (R)-1,1'-bi-{4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-methoxymethoxy}naphthyl (3)

[0061]

[Chemical Formula 31]



In an argon atmosphere, a 1.40M *tert*-butyllithium solution (1.93 mL, 2.7 mmol) was added dropwise to a tetrahydrofuran solution (10 mL) of Compound 2 (0.207 g, 0.30 mol) at  $-78^\circ\text{C}$  and the mixture was stirred for 15 minutes. Subsequently, dimethyl(perfluorooctyl)ethylchlorosilane (1.80 mmol) was added at  $-78^\circ\text{C}$ , and the reaction mixture was allowed

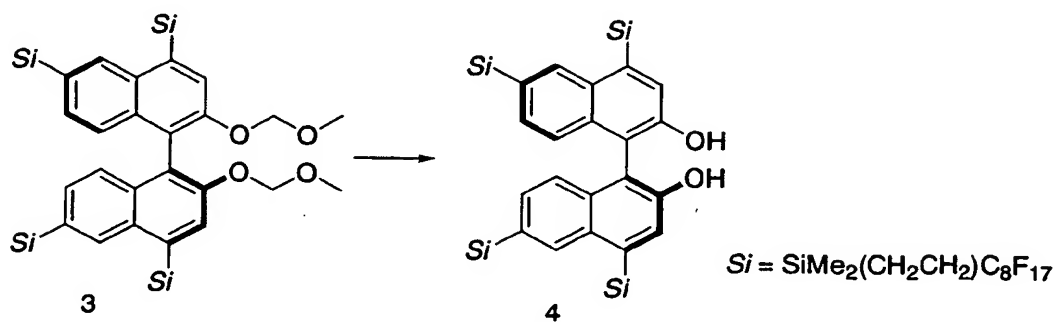
to warm to room temperature and was then stirred for 4 hours. After completion of the reaction, the reaction mixture was poured into water and was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of diethylether/hexane to give Compound 3 in a yield of 85%.

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.21 (2H, s, Ar-H), 7.74 (2H, s, Ar-H), 7.30 (2H, d, J = 8.4 Hz, Ar-H), 7.18 (2H, d, J = 8.4 Hz, Ar-H), 5.07 (2H, d, J = 6.8 Hz, Ar-OCH<sub>2</sub>), 4.95 (2H, d, J = 6.8 Hz, Ar-OCH<sub>2</sub>), 3.10 (6H, s, OCH<sub>3</sub>), 2.16-1.95 (8H, m, CH<sub>2</sub>CF<sub>2</sub>), 1.32-1.27 (4H, m, SiCH<sub>2</sub>), 1.02-0.98 (4H, m, SiCH<sub>2</sub>), 0.61 (12H, s, SiCH<sub>3</sub>), 0.37 (6H, s, SiCH<sub>3</sub>), 0.36 (6H, s, SiCH<sub>3</sub>).

Example 3 Synthesis of (R)-1,1'-bi-{4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-hydroxy}naphthyl (4)

[0062]

[Chemical Formula 32]



p-toluenesulfonic acid monohydrate (0.114 g, 0.60 mmol) was added to Compound 3 (0.30 mmol) in dichloromethane (10 mL)

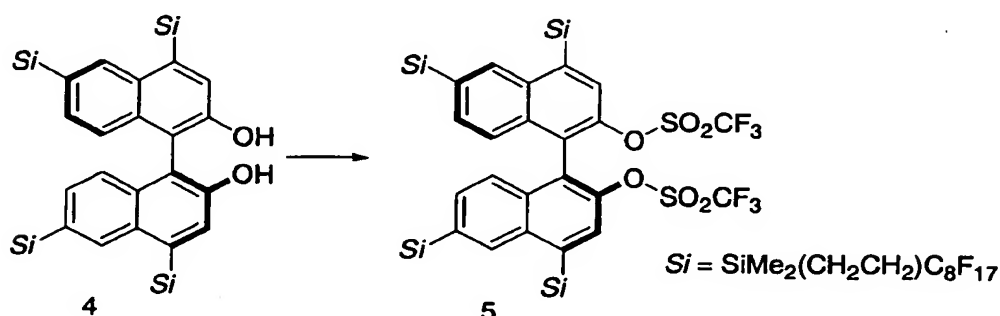
and methanol (10 mL) at room temperature, and the mixture was stirred at 50°C for 24 hours. After completion of the reaction, the reaction mixture was poured into water and was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure to give Compound 4 in a quantitative yield.

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>)  $\sigma$  8.23 (2H, s, Ar-H), 7.58 (2H, s, Ar-H), 7.39 (2H, d, J = 8.4 Hz, Ar-H), 7.20 (2H, d, J = 8.4 Hz, Ar-H), 5.01 (2H, s, OH), 2.13-1.97 (8H, m, CH<sub>2</sub>CF<sub>2</sub>), 1.33-1.28 (4H, m, SiCH<sub>2</sub>), 1.04-0.99 (4H, m, SiCH<sub>2</sub>), 0.61 (12H, s, SiCH<sub>3</sub>), 0.37 (12H, s, SiCH<sub>3</sub>).

Example 4 Synthesis of (R)-1,1'-bi-{4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-trifluoromethanesulfonyl}naphthyl(5)

[0063]

[Chemical Formula 33]



In an argon atmosphere, triethylamine (11.1 mmol) was added to a dichloromethane solution (25 mL) of Compound 4 (3.70 mmol), and the mixture was cooled to -78°C. Trifluoromethanesulfonic acid anhydride (11.1 mmol) was added

dropwise, and the mixture was allowed to warm to room temperature, followed by stirring for 1 hour. Subsequently, the reaction mixture was poured into a saturated aqueous solution of ammonium chloride and the solution was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the resulting residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of diethylether/hexane to give Compound 5 in a quantitative yield.

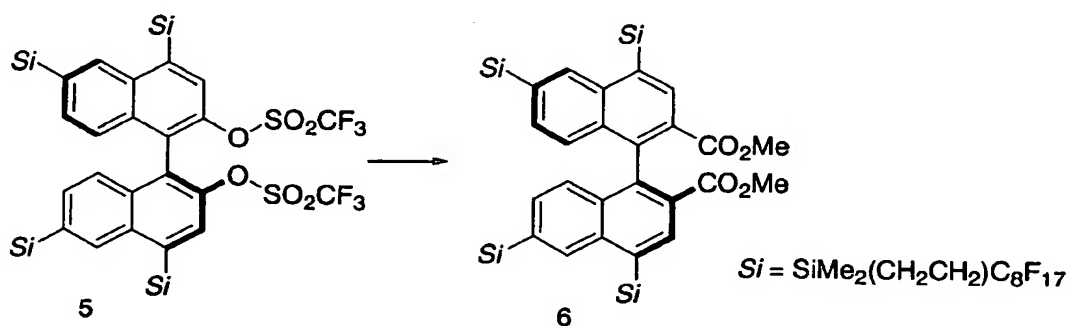
$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.33 (2H, s, Ar-H), 7.72 (2H, s, Ar-H), 7.47 (2H, dd,  $J = 1.2$  Hz, 8.4 Hz, Ar-H), 7.32 (2H, d,  $J = 8.4$  Hz, Ar-H), 2.05-1.87 (8H, m,  $\text{CH}_2\text{CF}_2$ ), 1.35-1.24 (4H, m,  $\text{SiCH}_2$ ), 1.05-1.01 (4H, m,  $\text{SiCH}_2$ ), 0.66 (6H, s,  $\text{SiCH}_3$ ), 0.64 (6H, s,  $\text{SiCH}_3$ ), 0.43 (6H, s,  $\text{SiCH}_3$ ), 0.41 (6H, s,  $\text{SiCH}_3$ ).

Example 5 Synthesis of (R)-1,1'-bi-{4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-methoxycarbonyl}naphthyl (6)

[0064]

[Chemical Formula 34]





In an argon atmosphere,  $i\text{Pr}_2\text{Net}$  (0.51 mL), MeOH (1.0 mL), and DMSO (2.0 mL) were added to a mixture containing Compound 5 (0.70 mmol),  $\text{Pd}(\text{OAc})_2$  (15 mol%), and dppp (16.5 mol%). While the reaction vessel was pressurized to 15atm under CO atmosphere, the mixture was stirred at 100°C for 24 hours. Subsequently, the reaction mixture was poured into water and the solution was extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the resulting residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of diethylether/hexane to give Compound 6 in a yield of 70%.

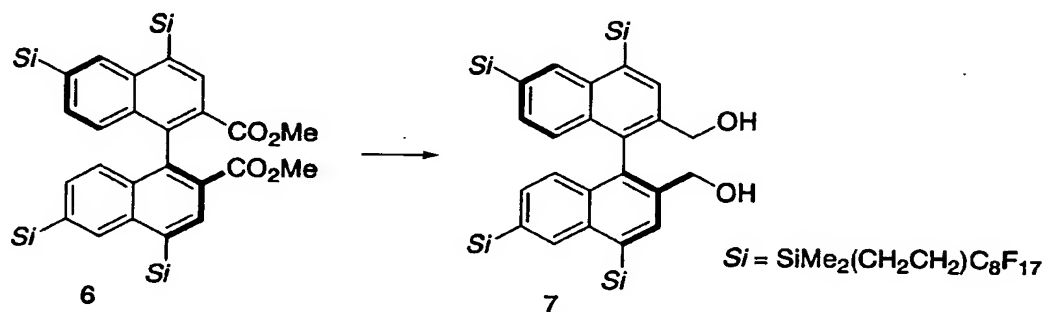
$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\sigma$  8.36 (2H, s, Ar-H), 8.29 (2H, s, Ar-H), 7.33 (2H, d,  $J = 8.4$  Hz, Ar-H), 7.23 (2H, d,  $J = 8.4$  Hz, Ar-H), 3.50 (6H, s,  $\text{CO}_2\text{CH}_3$ ), 2.18-1.93 (8H, m,  $\text{CH}_2\text{CF}_2$ ), 1.35-1.31 (4H, m,  $\text{SiCH}_2$ ), 1.04-1.00 (4H, m,  $\text{SiCH}_2$ ), 0.53 (12H, s,  $\text{SiCH}_3$ ), 0.38 (12H, s,  $\text{SiCH}_3$ ).

Example 6 Synthesis of (R)-1,1'-bi-{4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-hydroxymethyl}naphthyl

(7)

[0065]

[Chemical Formula 35]



5            In an argon atmosphere, Compound 6 (0.44 mmol) was added to a tetrahydrofuran solution of  $LiAlH_4$  (1.30 mmol) at  $0^\circ C$ , and the mixture was stirred for 1 hour. Subsequently, the reaction mixture was deactivated by sequentially adding MeOH and a saturated aqueous solution of ammonium chloride and the

10 solution was extracted with diethylether. The extract was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. The resulting residue was subjected to a silica gel column chromatography and eluted with a mixed solvent of diethylether/hexane to give Compound 7 in a

15 quantitative yield.

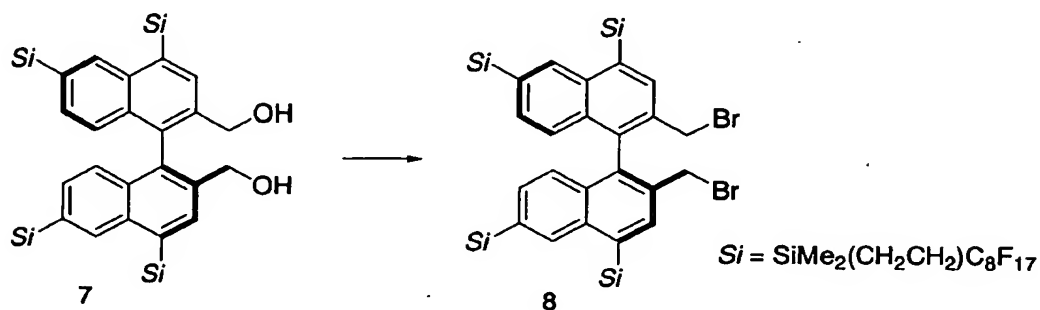
$^1H$ -NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.27 (2H, s, Ar-H), 7.90 (2H, s, Ar-H), 7.33 (2H, d,  $J = 8.4$  Hz, Ar-H), 7.10 (2H, d,  $J = 8.4$  Hz, Ar-H), 4.43 (2H, d,  $J = 11.6$  Hz,  $ArCH_2$ ), 4.14 (2H, d,  $J = 11.6$  Hz,  $ArCH_2$ ), 3.20 (2H, br s, OH), 2.16-1.98 (8H, m,  $CH_2CF_2$ ),

20 1.34-1.29 (4H, m,  $SiCH_2$ ), 1.06-1.01 (4H, m,  $SiCH_2$ ), 0.63 (12H, s,  $SiCH_3$ ), 0.37 (12H, s,  $SiCH_3$ ).

Example 7 Synthesis of (R)-1,1'-bi-{4,6-bis(2-perfluorooctylethyldimethylsilyl)-2-bromomethyl}naphthyl (8)

[0066]

[Chemical Formula 36]



5

Triphenylphosphine (0.315 g, 1.2 mmol) and carbon tetrabromide (0.398 g, 1.2 mmol) were added to a tetrahydrofuran solution (10 mL) of Compound 7 (0.20 mmol), and the mixture was stirred at room temperature for 4 hours.

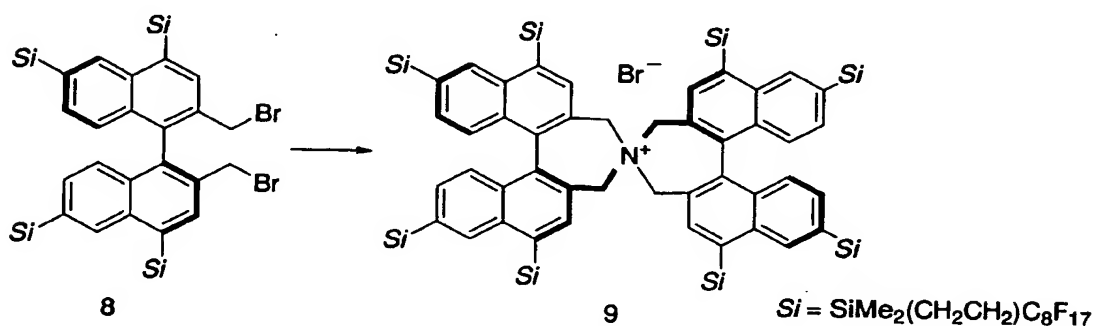
10 After completion of the reaction, the reaction mixture was poured into water and was extracted with dichloromethane. The dichloromethane solution was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the residue was subjected to a silica gel  
15 column chromatography and was eluted with a hexane solvent to give Compound 8 in a quantitative yield.

$^1H$ -NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.25 (2H, s, Ar-H), 7.89 (2H, s, Ar-H), 7.35 (2H, dd,  $J = 1.2$  Hz, 8.4 Hz, Ar-H), 7.09 (2H, d,  $J = 8.4$  Hz, Ar-H), 4.23 (4H, s,  $ArCH_2$ ), 2.17-1.97 (8H, m,  $CH_2CF_2$ ),  
20 1.34-1.25 (4H, m,  $SiCH_2$ ), 1.04-1.00 (4H, m,  $SiCH_2$ ), 0.64 (12H, s,  $SiCH_3$ ), 0.38 (12H, s,  $SiCH_3$ ).

Example 8 Synthesis of Spiro-bis-((R)-1,1'-bi-[4,6-bis(2-perfluorooctylethyldimethylsilyl)]naphthyl-2,2'-dimethyl}ammonium bromide (9)

[0067]

5 [Chemical Formula 37]



A 28% aqueous ammonia (0.77 mL, 12.6 mmol) and acetonitrile (5 mL) were added to Compounds 8 (3.15 mmol). The reaction vessel was sealed and the mixture was stirred for 24  
 10 hours while being refluxed. Subsequently, the reaction mixture was poured into water and the solution was extracted with dichloromethane. The extract was dried over anhydrous sodium sulfate and was concentrated under reduced pressure. After concentration, the resulting residue was subjected to a silica  
 15 gel column chromatography and eluted with a mixed solvent of dichloromethane/methanol to give Compounds 9.

$^1H$ -NMR (400 MHz,  $CDCl_3$ )  $\sigma$  8.41 (4H, s, Ar-H), 8.06 (4H, s, Ar-H), 7.39 (4H, d,  $J = 8.4$  Hz, Ar-H), 7.25 (4H, d,  $J = 8.4$  Hz, Ar-H), 4.48 (4H, d,  $J = 13.6$  Hz,  $ArCH_2$ ), 4.26 (4H, d,  $J = 13.6$   
 20 Hz,  $ArCH_2$ ), 2.20-1.98 (16H, m,  $CH_2CF_2$ ), 1.44-1.40 (8H, m,  $SiCH_2$ ),

1.07-1.03 (8H, m, SiCH<sub>2</sub>), 0.84 (12H, s, SiCH<sub>3</sub>), 0.79 (12H, s, SiCH<sub>3</sub>), 0.60 (12H, s, SiCH<sub>3</sub>), 0.43 (12H, s, SiCH<sub>3</sub>).

Example 9 Asymmetric alkylation using Compound (9) as optically active phase-transfer catalyst, recovery and recycle of the catalyst

[0068]

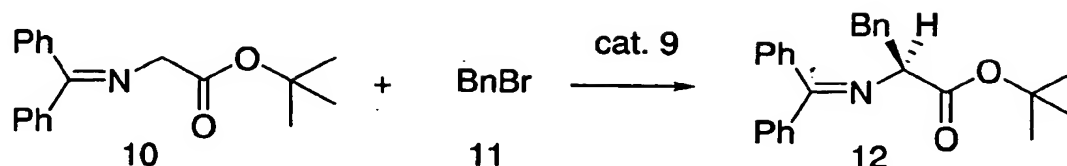
At 0°C and in an argon atmosphere, benzyl bromide (11) (0.36 mmol) was added to a toluene solution (3.0 mL) of Compound (10) of the general formula (12) (0.3 mmol) and Compound (9) of the general formula (1) (0.009 mmol). A 50% aqueous solution of potassium hydroxide (1.0 mL) was added dropwise and the mixture was vigorously stirred for 96 hours at the same temperature. Subsequently, the mixture was diluted with water (3.0 mL) and toluene (3.0 mL), and Compound (9) was extracted from the diluted solution with FC-72 (perfluorohexane) (3.0 mL x 3). The fluorous solvent was evaporated under reduced pressure and the remaining residue (quantitatively recovered for use as catalyst) was directly used in the subsequent reaction without further purification.

The crude product, which was a mixed solution of toluene/water containing Compound (12) as a primary component, was extracted with ether. The organic phase was washed with saturated brine, dried over sodium sulfate, and concentrated under reduced pressure. The residue was subjected to a silica gel column chromatography to give the alkylated compound 12. The results

are shown in Table 1.

[0069]

[Chemical Formula 38]



# 5 Example 10

Using the catalyst recovered in Example 9, the same process was repeated in the same reaction scale, followed by the same post-process. The results are also shown in Table 1.

[0070]

# 10 Example 11

Using the catalyst recovered again in Example 10, the same process was repeated in the same reaction scale, followed by the same post-process. The results are also shown in Table 1.

15 [0071]

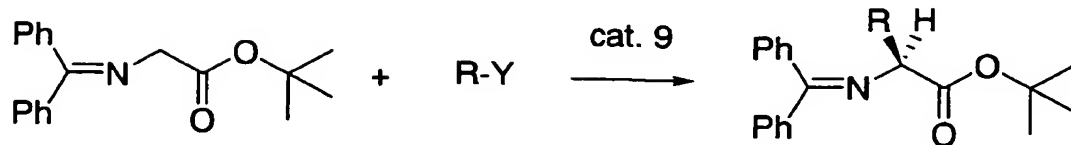
[Table 1]

	Catalyst 9 (Number of use)	Time (h)	Yield (%)	Optical Purity (%)
Example 9	First time	96	82	90
Example 10	Second time	96	79	92
Example 11	Third time	96	81	92

Examples 12 to 13 Asymmetric alkylation using Compound (9) as a phase-transfer catalyst

[0072]

20 [Chemical Formula 39]



Using Compound (9) as a catalyst, asymmetric alkylation was carried out in the same manner as in Example 9, except that a substrate shown as R-Y in Table 2 was used. The results are together shown in Table 2.

[0073]

[Table 2]

	R-Y	Time (h)	Yield (%)	Optical Purity (%)
Example 12	CH <sub>2</sub> =CHCH <sub>2</sub> Br	142	80	84
Example 13	HC≡CCH <sub>2</sub> Br	140	81	90

The optical purity of the reaction products was determined according to the technique described in *J. Am. Chem.*

*Soc.* 1999, Vol. 121, No. 27, 6519-6520.

[TITLE OF DOCUMENT] Abstract

[Object]: There is provided a novel optically active quaternary ammonium salt that is a high performance axially chiral spiro phase-transfer catalyst used in the asymmetric alkylation of a glycine derivative, and in which each ring of the spiro-structure has the same structure that is advantageous in terms of the number of steps involved in the synthesis of the catalyst, and a method for producing the same and a method for recovering, and purifying the same.

[Solving means]: To achieve the objects, an axially chiral spiro-ammonium salt that incorporates a substituent encompassing a perfluoro alkyl group, which is excellent in phase-transfer catalyst, the ammonium salt is used in the asymmetric alkylation of a glycine derivative and thereafter is recovered and purified using a fluoruous solvent without degrading the performance of catalyst.